UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/512,260	02/24/2000	Lynn M. Adams	03037.86702	5959

22907 7590 05/07/2002

BANNER & WITCOFF
1001 G STREET N W
SUITE 1100
WASHINGTON, DC 20001

EXAMINER	
DEBERRY, REGINA M	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 05/07/2002 10

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/512,260	ADAMS ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *8-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Status of Application, Amendments and/or Claims

The information disclosure statement filed 23 August 2000 (Paper No. 4) was received and complies with the provisions of 37 CFR §§1.97 and 1.98. It has been placed in the application file and the information referred to therein has been considered as to the merits.

The amendment filed 05 February 2002 (Paper No. 9) has been entered in full. Applicant's election of Group I (claims 1-7) in Paper No. 9 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 8-34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 9.

Specification

The drawings are objected to because they are mislabeled. "Figure 1" should be labeled "Figure 2" and "Figure 2" should be labeled "Figure 1".

The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they do not include the following reference sign(s) mentioned in the description: 4A, 4B and 4C. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code on pages 8 and 10. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 7 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 7 is drawn to the polypeptide of claim 1 which is free of phosphorylation. Claim 1 is drawn to an isolated polypeptide comprising a portion of cystic fibrosis transmembrane conductance regulator (CFTR) protein of between 10 and 100 amino acids, said portion comprising 18 amino acids as shown in SEQ ID NO:1 and a polypeptide which comprises 22 amino acids as shown in SEQ ID NO:2.

The specification states that the opening of the CFTR channel is controlled by PKA phosphorylation of serine residues in the R domain and ATP binding and hydrolysis at the NBFs. Phosphorylation adds negative charges to the R domain, and introduces global conformational changes reflected by the reduction in the α-helical content of the R domain protein. Thus, electrostatic and/or allosteric changes mediated

by phosphorylation are likely to be responsible for interactions between R domain and other CFTR domains that regulated channel function (page 1, line 22-page 2, line 8). The specification cites art which suggests that unphosphorylated R domain is inhibitory and phosphorylated R domain is stimulatory (page 2, lines 15-23). The specification teaches that about 25% of the known 700 mutations in CFTR produce a mutant CFTR protein which is properly transported to the apical membrane of the epithelial cells but have only low level residual channel activity. There is a need in the art for agents which can boost the level of channel activity in those mutants having low level activity (page 2, line 24-page 3, line 4). The specification states that, "it is an object of the present invention to provide an isolated polypeptide useful for enhancing the open probability of the CFTR chloride channels" (page 3, lines 6-7). The specification also cites methods for activating a CFTR protein. It is therefore unclear, how to use the instant polypeptide which is free of phosphorylation because the specification does not teach how to use an isolated unphosphorylated peptide comprising a portion of CFTR.

Due to the large quantity of experimentation necessary to discern how to use an isolated unphosphorylated peptide comprising a portion of CFTR, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the prior art which states that unphosphorylated R domain is inhibitory and phosphorylated R domain is stimulatory and the breadth of the claims which fail to recite limitations regarding phosphorylation, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 102

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1 and 2 are rejected under 35 U.S.C. 102(e) as being anticipated by Tsui *et al.* US Patent No. 5,776,677. The instant claims are drawn to an isolated polypeptide comprising a portion of cystic fibrosis transmembrane conductance regulator (CFTR) protein of between 10 and 100 amino acids, said portion comprising 18 amino acids as shown in SEQ ID NO:1 and a polypeptide which comprises 22 amino acids as shown in SEQ ID NO:2. Tsui teaches a CFTR protein (100% identical) comprising the amino acid sequences in SEQ ID NO:1 and SEQ ID NO:2 of the instant application. (Please see sequence query, Appendix A and B).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsui *et al.* US Patent No. 5,776,677 in view of Welsh *et al.* WO 95/25796 (IDS, Paper No. 4) and Langel *et al.* US Patent No. 6,025,140. Claims 3-6 are drawn to polypeptides fused to membrane-penetrating peptides. Tsui teaches a cystic fibrosis protein (100% identical) comprising the amino acid sequences in SEQ ID NO:1 and SEQ ID NO:2 of the instant application. Tsui does not teach the fusion of the instant sequences to a membrane penetrating peptide or membrane penetrating peptides wherein the sequence is SEQ ID NO:3, SEQ ID NO:4 or SEQ ID NO:5.

Welsh teaches truncated forms of cystic fibrosis transmembrane conductance regulator polypeptide (page 14, lines 21-23). Welsh teaches that truncated CFTR polypeptide can be administered alone or in association with an agent that facilitates passage (via fusion or endocytosis) through cell membranes to the effected cells (page 32, line 22-25). Welsh teaches the use of fusion proteins comprising CFTR (page 33, line 14-page 14, line 4).

Langel teaches membrane-penetrating peptide sequences which are 100% identical to SEQ ID NO:4 and SEQ ID NO:5 of the instant application. (Please see sequence query Appendix C and D and specification, column 15, lines 1-2). Langel teaches constructs of peptides and nucleic acid analogs conjugated together for transport across a lipid membrane (abstract, column 5, lines 46-54 and claims). Langel teaches the use of these peptides in drug delivery (column 16, lines 19-37).

It would be obvious to one skilled in the art at the time the invention was made to modify a cystic fibrosis protein comprising the amino acid sequences in SEQ ID NO:1 and SEQ ID NO:2 of Tsui *et al.* by using the teaching of Welsh and Langel regarding fusion and membrane-penetrating peptides to make a fusion protein. The motivation and expected is provided by Welsh who teaches fusion proteins comprising CFTR and Langel who teaches that the fusion of a protein with membrane-penetrating peptides can facilitate the uptake by target cells.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (703) 305-6915. The examiner can normally be reached on Mondays-Fridays 8:00 a.m. - 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-7939 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

RMD

RMD
May 2, 2002

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER